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PROLONGED EXPERIMENTAL FEBRILE SEIZURES IN IMMATURE RAT CAUSE SPONTANEOUS BEHAVIORAL AND ELECTROPHYSIOLOGICAL SEIZURES DURING ADULTHOOD

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Rationale: Experimental prolonged febrile seizures lead to structural and molecular changes that promote hippocampal hyperexcitability and reduce the threshold to further convulsants. However, whether these early-life 'prolonged febrile' seizures lead to spontaneous seizures (epilepsy) later in life has remained unclear. Previously, daytime video-EEG monitoring did not reveal spontaneous seizures in adult rats subjected to experimental prolonged febrile seizures during infancy. Because limbic seizures may vary diurnally and may be behaviorally subtle, we determined here the presence of *nocturnal* spontaneous limbic seizures, using chronic nocturnal hippocampal EEGs combined with videos.

Methods: Experimental prolonged febrile seizures were induced on postnatal day (P)10. Digital video EEG monitoring was performed chronically at night in control ($n = 9$) and experimental ($n = 17$) rats carrying unilateral bipolar hippocampal and cortical electrodes. Starting on P70, each rat was recorded for a total of 6 nights over 3 months. EEGs were analyzed blindly for the presence of limbic seizures, and correlated with concurrent videotaped behavior.

Results: EEGs were normal in all control rats, and none developed spontaneous seizures. Spontaneous behavioral and EEG seizures were found in 31% of experimental rats, and seizures averaged 7.1 ± 0.8 seconds. An additional 9 rats (56%) did not become epileptic but demonstrated abnormalities on nocturnal EEGs, consisting interictal bursts of spikes. Three experimental rats (13%) had no evidence of EEG or behavioral abnormalities.

Conclusions: Prolonged experimental febrile seizures in immature rats result in spontaneous seizures (limbic epilepsy) later in life in a significant proportion of subjects, and to abnormal EEGs in the majority. Understanding how these experimental febrile seizures lead to epilepsy, i.e., the mechanisms of this epileptogenic process, should yield molecular targets for epilepsy prevention. [Supported by an NIH grant 35439 (T.Z.B.) and by an Epilepsy Foundation of America postdoctoral research fellowship (C.D.).]